

### REMARKS

Favorable reconsideration of this application, as presently amended and in light of the following discussion, is respectfully requested.

Claims 1, 3-6, and 9-18 are currently pending. Claims 1 and 3-15 have been amended; Claim 2 has been cancelled without prejudice or disclaimer; and Claims 16-18 have been added by the present amendment. Support for amended Claims 1 and 3-15 and new Claims 16-18 can be found at least at page 11, lines 5-9; page 13, lines 15-24; and page 16, line 25-27 of the specification. No new matter is added.

In the outstanding Office Action, the specification was objected to as containing informalities; Claims 1, 3-5, and 9-15 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2004/0033166 to Arnowitz (hereinafter “the ‘166 application”) in view of WO Publication No. 99/27349 to Gaillon et al. using U.S. Patent No. 6,723,554 as the closest English translation (hereinafter “the ‘554 patent”); Claim 2 was rejected under 35 U.S.C. § 103(a) as being unpatentable over the ‘166 application in view of the ‘554 patent and U.S. Patent No. 6,307,630 to Bannerjee (hereinafter “the ‘630 patent”); and Claim 6 was rejected under 35 U.S.C. § 103(a) as being unpatentable over the ‘166 application in view of the ‘554 patent and U.S. Patent No. 5,814,277 to Bell (hereinafter “the ‘277 patent”).

In response to the objection to the specification that the Abstract includes legal phraseology such as “means,” Applicants have amended the Abstract to remove references to terms such as “means.” Thus, Applicants respectfully submit that the outstanding objection is rendered moot by the present amendment to the Abstract.

In response to the rejection of Claims 1, 3-5, and 9-15 under 35 U.S.C. § 103(a) as being unpatentable over the ‘166 application in view of the ‘554 patent, Applicants

respectfully submit that amended independent Claims 1 and 9 recite novel features clearly not taught or rendered obvious by the applied references.

Amended Claim 1 is directed to an automated and robotized platform including a battery of micro-fermentors including, *inter alia*:

...an external sensor configured to measure an optical property of each cell culture contained in each micro-fermentor, the external sensor including a turbidity-measuring sensor, ***the turbidity-measuring sensor including an emitting diode and a receiving diode***;

...a system configured to regulate a temperature ***of each micro-fermentor including a Peltier effect autonomous regulating system***, the regulation of the temperature by Peltier effect being independent and programmable for each micro-fermentor, ***at a temperature range of -5°C to 80°C***.

By way of background, a non-limiting embodiment of Applicants' invention, as described at page 29, lines 4-11 of the specification, allows for the cultivation of cells at a temperature with an optimum growth rate, such as 30°C or 37°C, to quickly obtain a biomass followed by an automatic temperature decrease at 15°C or less if required. In this non-limiting example, the temperature can be brought back to, for example, 4°C to maintain the culture in optimum processing waiting conditions as may be desirable in the case of night cultures.

Regarding the rejection of Claim 1, the Office Action asserts that the '166 application discloses all of the features of Claim 1 with the exception of a micro-fermentor having a useful culture volume ranging from 2 mL to 500 mL and relies on the '554 patent to remedy that deficiency.

The '166 application discloses a fluid transfer mechanism 26 that supplies a liquid reagent from a reagent reservoir 28 to a dynamic dialysis unit 36. A temperature controller 38 is provided at the fluid circuit to control the temperature of a reagent that is pumped from the mechanism 26 to the unit 36. The temperature controller 38 may include a Peltier

device.<sup>1</sup> The '166 application also discloses that cell culture chambers are maintained at a temperature of 37°C by blowing warmed air through the magnet bore. Temperature is monitored with thermocouples in the magnet bore.<sup>2</sup> The '166 application includes a single reference to turbidity and only discloses that static light scattering permits turbidity measurements.<sup>3</sup>

Page 4 of the Office Action asserts that the camera disclosed at paragraph [0122] of the '166 application is "fully capable of measuring turbidity," and that this camera reads on the turbidity-measuring sensor recited in Claim 1.

However, as noted above, turbidity is mentioned only once in the entire disclosure of the '166 application at paragraph [0230], where static light scattering is disclosed as permitting turbidity measurements. The '166 application fails to disclose a camera obtaining any turbidity measurement. Thus, the camera of the '166 application fails to read on the turbidity-measuring sensor recited in Claim 1.

Additionally, the '166 application fails to disclose a system configured to regulate a temperature *of each micro-fermentor* including a Peltier effect autonomous regulating system or regulation of temperature being independent and programmable at a range of -5°C to 80°C. The Office Action asserts that paragraph [0100] of the '166 application reads on the Peltier effect autonomous regulating system recited in Claim 1. As noted above, the Peltier system disclosed at paragraph [0100] of the '166 application is directed to regulating a temperature of *reagents*. In contrast, amended Claim 1 recites that the system is configured to regulate a temperature of *each micro-fermentor* including a Peltier effect autonomous regulating system. The '166 application fails to disclose Peliter devices used to regulate the temperature of a micro-ferementor.

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<sup>1</sup> See paragraph [0100] of the '166 application.

<sup>2</sup> See paragraph [0181] of the '166 application.

<sup>3</sup> See paragraph [0230] of the '166 application.

Further, as noted above, the '166 application specifically recites the use of a **heating system** to blow hot air on a magnet bore to maintain a temperature of cell culture chambers. The '166 application does not disclose the use of any Peltier devices for the cell cultured chambers. Thus, the system of the '166 application is only capable of **heating** its cell cultured chambers and cannot cool them. In contrast, amended Claim 1 recites that the regulation of the temperature of each micro-fermentor is independent and programmable **at a temperature range of -5°C to 80°C**.

It is respectfully submitted that the '554 patent is silent as to temperature regulation.

Thus, no matter how the teachings of the '166 application and the '554 patent are combined, the combination does not teach or suggest "a system configured to regulate a temperature of each micro-fermentor including a Peltier effect autonomous regulating system, the regulation of the temperature by Peltier effect being independent and programmable for each micro-fermentor, at a temperature range of -5°C to 80°C," as recited in amended Claim 1.

In the rejection of Claim 2, the Office Action acknowledges that the '166 application and the '544 patent fail to disclose a turbidity sensor including an emitting diode and a receiving diode, and relies on the '630 patent to remedy this deficiency. Claim 1 has been amended to recite this subject matter of previous Claim 2.

However, Applicants respectfully submit that there is no motivation to combine the teachings of the '630 patent with the '166 application and the '544 patent.

The '630 patent is directed to turbidimeters used in monitoring turbidity of drinking water.<sup>4</sup> Column 1, lines 46-47 of the '630 patent disclose that instruments generally lack sensitivity to sub-micron particles. Thus, the disclosure of the '630 patent is directed towards **detecting sub-micron particles**. It is respectfully submitted that one of ordinary skill in the

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<sup>4</sup> See Abstract of the '630 patent.

art, seeking to modify the '166 application to detect turbidity of cell cultures would not select the turbidimeter of the '630 patent directed to detecting submicron particles, as this scale of measurement is not consistent with the size of suspended cell particles in a cell culture.

Thus, it is respectfully submitted that the Office Action has failed to present a *prima facie* case of obviousness of Claim 1 as no proper motivation to combine the teachings of the '630 patent with the teachings of the '166 application and the '544 patent has been provided.

Independent Claim 9, although varying in scope and statutory class, patentably defines over the '166 application, the '544 patent, and the '630 patent at least for reasons analogous to the reasons stated above for the patentability of independent Claim 1.

Regarding the rejection of dependent Claim 6, Applicants note that Claim 6 is dependant on independent Claim 1, and is patentable at least for the reasons described above. Further, Applicants respectfully submit that the '277 patent fails to cure any of the above-noted deficiencies of the '166 application, the '554 patent, and the '630 patent.

Accordingly, Applicants respectfully submit that the rejections of Claims 1 and 9 (and all claims depending thereon) under 35 U.S.C. § 103(a) are rendered moot by the amendments to independent Claims 1 and 9.

Additionally, Applicants respectfully submit that neither the '166 application, the '554 patent, the '630 patent, the '277 patent, nor any proper combination thereof teaches or suggests the subject matter of new Claims 16 and 17.

For example, new Claim 17 recites that “the sampling and injecting system is configured to increase O<sub>2</sub> concentration or *inject solutions configured to regulate pH in response to a measurement of the optical property.*” The '166 application discloses that the rate of medium exchange necessary to maintain a constant pH *can be determined empirically by a person of ordinary skill.*<sup>5</sup> The '166 application is silent as to an O<sub>2</sub> concentration.

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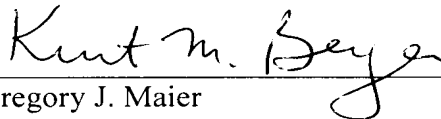
<sup>5</sup> See paragraph [0183] of the '166 application.

Thus, the '166 application fails to read on the sampling and injecting system recited in Claim 17. The '554 patent, the '630 patent, and the '277 patent are silent as to an O<sub>2</sub> concentration or a pH. Thus, no matter how the '166 application, the '554 patent, the '630 patent, and the '277 patent are combined, the combination does not teach or suggest a "sampling and injecting system is configured to increase O<sub>2</sub> concentration or inject solutions configured to regulate pH in response to a measurement of the optical property," as recited in Claim 17.

Consequently, in view of the present amendment, and in light of the above discussion, the outstanding grounds for rejection are believed to have been overcome. The pending claims as amended herewith are believed to be in condition for formal allowance. An early and favorable action to that effect is respectfully requested.

Respectfully submitted,

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